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Across the centuries: Piecing together the anatomy of the heart

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ABSTRACT

Background: The history of the cardiac anatomy dates back to 3500 B.C. when the Greeks and Egyptians based their understanding of this structure on their religious beliefs. During the 5th century, Hippocrates, the “Father of medicine,” established medicine as a science and highlighted the principles of medical knowledge, replacing these previous tenets.
Methods: This literature review seeks to collate and discuss peer-reviewed articles on the history of cardiac anatomy.
Results: Advances in the understanding of the structure, location and function of the heart occurred during the post-Hippocratic era. Upon establishment of its anatomic structure, the interconnection between the heart and the lungs was sought and the pulmonary circulation was described. After the first description of the heart as a pump was made, it was followed by the innervation of the cardiac system, as well as a description of the conducting system in the eighteenth, nineteenth and twentieth centuries.
Conclusion: The history of the cardiac anatomy was widely influenced by intellects of varying backgrounds, which led to significant contributions to our current understanding.

1. Introduction

The gross anatomy of the heart has taken centuries to piece together. From Hippocrates to Galen to Leonardo da Vinci, great anatomists, philosophers, and even artists have contributed to demystifying the puzzle which was once the structure of the heart. Ancient intellects fought against religious and cultural restrictions to provide us with the basis on which we have built our sciences and more so, medicine. Despite the strides that have been made in understanding the anatomy of the heart, recent anatomists have made new findings. This manuscript examines the history of cardiac anatomy, from its birth to its maturation and reviews its current attitudinal refinement.

2. 19th - 16th century B.C

While the Greek antiquity dominates the early historical accounts of anatomy, the first written evidence of the use of anatomical terms and physiological concepts dates back to around 1600 - 1900 BCE. This knowledge is contained in the ancient “Egyptian medical papyri,” most notably: the (Edwin) Smith Papyrus, the (Georg) Ebers Papyrus, and the (Heinrich) Brugsch Papyrus, also known as the Greater Berlin Papyrus. The Smith Papyrus is believed to have originated from a more archaic document that was probably written around 3000-2500 BCE [1]. The Ebers Papyrus documents the heart and the great vessels. Similarly, the Ebers Papyrus contains a description of the heart [2].

In the ancient world, the social construct was established by the tripartite principles of religion, magic, and medicine. It was believed that the heart acted as a recorder of deeds done during one's life. After death, judgment was rendered based on the weighing of the heart against a feather. Eternal salvation was afforded to those whose heart was light and thus considered virtuous, versus that of a heavy heart forever damned an individual [2]. Even in life, the heart was highly recorded by the Egyptians as it was considered to be central organ of thought, emotion, bodily fluid, e.g., urine, feces, diseases and the “metw” (soul) [3,4].

Since human dissection was not practiced, the Egyptians relied on observations from the mummification process, and veterinary dissection to decipher the anatomy of the body. They quickly recognized the

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heart as the center of the cardiovascular system, where it was connected with several other organs to receive water and air [3]. They also recognized that the "vasculature" extended to the limbs, often confusing other structures such as veins, tendon, nerves for "metw" (vessels). Furthermore, due to the lack of human dissection, they perceived that the various bodily fluids entered into different organs [3]. No records have been found with regards to the Egyptians' knowledge or lack of the specific structures of the heart [5].

3. 6th century B.C

For almost 1000 years after the production of the papyri, it is claimed that no medical manuscripts were produced. Some authors contend that this resulted from the repeated wars and invasions which devastated the region [6]. While others suggest that the practice of medicine had become a largely oral tradition [2].

With the reconstruction of the destroyed great temples of Egypt, the "house of life" was constructed and attached to the temple. This house was used for the training of priest-physicians in rational medicine and mysticism. These teachings were secretive and so they were conveyed orally [2].

4. 5th century B.C

"καρδία" or "καρδιά" is the ancient Greek word for the heart. Some conceive that this word originated from the belief that the heart carried the soul, while others suggest that it originated from the Greek verb "κραδαίνω," which means to move continuously [7].

Asclepios, a Greek wound-healing physician, is considered to be one of the first to possess significant anatomical knowledge as it relates to the cardiovascular system. However, there are no written records which corroborate this fact [5].

The 5th century represented an epoch in the medical world as Hippocrates, who would come to be known as the "Father of medicine," introduced concepts of medical thinking and ethics. These concepts of medical thinking permanently established medicine as science versus its previous tenets which saw it shrouded in religious, philosophical and mystical principles [7]. In addition to these new concepts regarding medicine, Hippocrates, either with or without his followers, contributed the Hippocratic Corpus. The Hippocratic Corpus is a series of 70 books which established principles of medical knowledge [8].

Of particular interest is a book entitled, "Περί καρδίης", which translates to "On the Heart." This book details the topographic anatomy of the heart, without any philosophical conjectures. For the time in which it was written, such a purely anatomical work can be considered revolutionary. However, despite its scientific genius, with regards to the cardiac anatomy, some of its details are incorrect and/or unclear [7]. The author of "On the Heart" alluded to the two ventricles in his description of "γαστέρας," which means abdomens. He appreciated and documented the wall and dimensional differences between the two "abdomens" [7]. He postulated that these differences were due to the fact that the left ventricle was the heat generator and site of pure air of life "pneuma" [5]. He was the first to describe the valves, in particular, the semilunar valves of the pulmonary artery and aorta. The author also described the auricles, which, based on the shape, the Greek word for ears: "ούατα" was given. The auricles were not perceived as an anatomical structure of the heart itself, but rather, recognizing there was no channel for the reception of sound, he concluded that the auricles received air instead of sound [9]. Based on his anatomical observations, he offered possible physiological explanations most of which were incorrect [7].

It should be noted that while "On the Heart" is considered a Hippocratic treatise, some authors hold that it post-dates Herophilus of the 3rd century. Similarly, two other works of the Hippocratic Corpus: "On Nutriment" and "On Joints" which offer a distinction of the arteries vs. veins are considered to postdate Herophilus [10]. With regards to the books of the Hippocratic Corpus which with certainty predates Herophilus, no consensus on the vascular system was reached. One noteworthy Hippocratic treatise is "On Fleshes," which recognizes the heart as the central source of blood vessels, with all vessels culminating into two vessels: "the artery and hollow vein," both which originated from the heart. However, this is contradicted by another Hippocratic treatise which regards the head as the origin of the vessels [10].

Another notable physician of the fifth century was Alcmaeon (a pre-Socratic physician and philosopher); he is regarded as the first to perform animal dissections, however, this remains a contentious topic. He is also credited as the first to vaguely recognize the difference between arteries and veins, that is without recognition of their anatomical differences [5,7]. Moreover, he is also regarded as the first to describe some aspect of the circulation of blood [7]. During the 5th century, there was much disagreement between the head and the heart as it related to the center and origin of blood vessels [10]. The majority conceded that the head played this role, Alcmaeon also held this belief. He further postulated that the circulating blood into the cerebral vessels were associated with sleep and death [7].

In this era, concepts regarding the cardiovascular system were also influenced by Empedocles, a physician, philosopher and poet [7]. Empedocles was the first to recognize that the heart formed prior to any other organ [5]. According to Mavrodi and Paraskevas [7], with regards to the heart versus head debate, Empedocles fell in opposition to Alcmaeon as he thought the heart was the center of the cardiovascular system and the origin of the soul and mind. Empedocles theorized that blood was used to distribute "pneuma" to the whole body, a theory which would come to be known as "pneumatism". Pneuma refers to the spirit of life, which is said to mobilize the organism [7]. However, von Staden [10] holds that while Empedocles highly regarded the blood and its value to the body, he offered no connection of the blood vessels to the heart or details regarding the organ itself. Instead, Empedocles theorized that blood "ebbed and flowed" in the vessels to eventually open into the pores of the skin. This anatomical description was used to support the theory of 'portal' cutaneous respiration [10].

Like many of his time, Diogenes of Apollonia also supported the "pneumatism" theory. Diogenes tried to describe the vascular system; however, he mistakenly concluded that it was made up of only "φλέβες" - veins [7].

5. 4th century B.C

A few years after, Hippocrates, Syennesis of Cyprus, tried to offer the first anatomical description of the vessels. However, Syennesis thought that the vessels originated from the umbilicus, instead of the heart [7]. The central role of the heart finally began to pick up support with Plato's description in the Timaeus. In the book mentioned above, the heart is regarded as a "knot of veins and a source of the blood which races through the limbs …" However, it was not until Diocles of Carystus that details of the heart as the center and origin of the blood vessels were recorded [10]. Diocles of Carystus was regarded as "the younger Hippocrates; " he is considered the first to use animal dissections to write an anatomical textbook. However, all of his original works have been lost, leaving historians to piece together his accomplishments based on the writings of other authors [7]. In his works, Diocles of Carystus is said to have commented on the two "auricles" of the heart. In perceiving the ear-like structure of the auricles, Diocles of Carystus concluded that the heart had cognitive powers [9].

6. 3rd century B.C

Aristotle is one of the greatest philosophers and scientists ever to live. He used animal dissections to further his understanding of the human anatomy. In particular, he had a vested interest in the anatomy of the heart, which he documented in great detail. However, even his works contained errors as his only human dissection was that of a 40-

day-old fetus. Aristotle erroneously located the heart inferior to the carina, with variable locations depending on the size of the animal [7]. Based on the findings in animals, Aristotle wrongly held that the heart of humans, like all animals, had three ventricles. Aristotle also identified ducts connecting the lungs and the heart, these vessels which were thought to carry the "breath of life," more than likely referred to what we know now as the pulmonary arteries and veins. In attempting to describe the vena cava and the pulmonary artery, Aristotle conceived that a "large vein" divided to give two branches to the right ventricle. He also offered a description of the aorta [7]. He recognized two vascular systems: a pneumatic made up of arteries; and a hematic, made up of veins [10]. Aristotle also observed the presence of the tendinous chordae and papillary muscles. However, he incorrectly identified them as "nerves" [9]. The greatest miscue Aristotle made was his conclusion that, in addition to being the source of the vessels [5], the heart was also the source of the nerves, with the aorta tapering off to wholly become nervous tissue [7]. However, despite this blunder, Aristotle correctly concluded, like Diocles of Carystus before him, that the blood vessels originated from the heart. Thus, Aristotle was essential in forwarding the cardiocentric theory [7].

Praxagoras of Cos strongly supported Aristotle's cardiocentric theory. In addition to recognizing the heart as the origin of the cardiovascular system, this theory also held that the heart generates a heat which houses the soul and thought [7]. Praxagoras is credited with being the first to offer a clear functional distinction between arteries and veins, that is based on the material they carried [5]. However, he wrongly postulated that the arteries carried air, while veins carried blood [7]. Philosophers and physicians of this time who supported this distinction also recognized that vessels emerging from the right ventricle were called veins (phlebes), versus those originating from the left ventricle were known as arteries (artēriai) [10]. Due to Aristotle's writings, Praxagoras also thought that the arteries narrowed to become nerves [5].

In the latter part of the 3rd century, under the mentorship of Praxagoras, Herophilus became known as the "Vesalius of antiquity," in other words, the "Father of Anatomy" [7]. He was able to make great strides in Anatomy as he studied in the 30–40 years in which human dissections were permitted; thus, he is regarded as the first anatomist [11]. Prior to Herophilus and Erasistratus, human dissection for anatomical purposes was not permitted due to religious and/or cultural convictions, such as, the belief that the corpse was a pollutant for anyone and anything that came into contact with it. On another note, the skin was regarded as: a sacred symbol for the invisible "skin" that enveloped the community and fostered togetherness; a natural limit which like other natural limits should not be crossed; and an external manifestation of the internal physical and moral standing of an individual [12]. However, due to their royal patronage, in addition to their location in Alexandria (an intellectual hub which valued scientific advancement and was known to break Greek traditions), Herophilus and Erasistratus were able to forward the knowledge of human anatomy and physiology through dissections, and perhaps even vivisection [12,13]. This opportunity wouldn't be afforded to physicians again until the middle ages [13].

Herophilus rejected the "cardiocentric" theory and instead proposed that the cerebellum and spinal cord were the origins of the nervous system. Moreover, Herophilus furthered the work of his mentor as he was able to go beyond the proposed "physiological" difference, and instead provided an anatomical distinction between the arteries and veins based on the characteristics of their walls. Thus, he was able to, partially at least, correct the misconception that all vessels originating from right ventricle were veins as he described the now known pulmonary artery as an "artery-like vein" or "arterial vein" [10]. Furthermore, he recognized the pulmonary vein as a "vein-like artery," also referred to as a "venous artery" [5]. Herophilus did not remain confined to the heart but documented vessels in several areas of the body including the head, thorax, abdominal cavity, and reproductive systems. Of particular note is that Herophilus' description of blood supply to the liver is thought to have laid the foundation for the understanding of the physiology of the liver [10]. Herophilus is also credited with recognizing the "atria" as anatomically components of the heart versus the previously school of thought which held that the "atria" were dilatation of the great vessels [7]. Moreover, in contrast to his contemporary, Herophilus recognized the auricles as an internal feature of the heart [9,10]. Thus, he was one of the first to recognize that the heart is a composite of four chambers [5]. According to Galen, Herophilus also noted the presence of the tendinous chordae and papillary muscle, to which he referred to as "neural diaphyses" [9]. Sadly, Herophilus' work has been lost as much of it has been coveted by other writers [7].

As Herophilus made key advances in anatomy, Erasistratus focused on the physiology of the heart. He is credited with the recognition that the structure of the heart is well suited for its function as a pump. Moreover, Erasistratus was the first to describe of all the valves. Based on their shapes, he attributed the description "sigmoid" to the valves of the arterial vein (the pulmonary artery) and aorta [7,14]. However, according to Paraskevas, Koutsouflianiotis, and Iliou [9], Galen is the one responsible for the naming of the arterial valves as "semilunar or sigmoid (cusps)." Erasistratus also characterized the atrioventricular valves based on their number of cusps [7]. More notably, he is considered the first to provide an accurate interpretation of the functions of the valves as unidirectional gates [9]. Erasistratus was the first to describe the circulatory system recognizing the heart as the origin of all vessels, with the end of the veins representing the anatomical beginning of the arteries. He also stated that the veins drained into the right ventricle, while the arteries connected with the left ventricle [7]. Moreover, Erasistratus described the circulation from the liver to the heart via the inferior vena cava, and then from the heart to the lungs via the arterial vein (pulmonary vein) [15]. However, despite his advances in recognizing the anatomical structure of the circulatory system, he wrongly held on to the "pneumatic" theory. As a result, he furthered the theory that the arteries carried air, and so named the left ventricle "pneumatic." He also incorrectly disregarded Herophilus' recognition of the "atria" as anatomical components of the heart and held onto the previous arterial dilation theory [7].

7. 2nd century B.C

During the 2nd century, significant advances in cardiac anatomy were made thanks to Claudius Galen. Through his astute dedication to learning and knowledge, Galen became a distinguished physician in Greek-Roman medicine [16]. He built on the works of highly acclaimed physicians before him such as Erasistratus of Chios and Hippocrates, while distancing himself from Aristotle's principles [7]. Galen offered descriptions of the heart's shape; the pericardium; the position of the great vessels, in particular: the arterial vein (pulmonary artery), the aorta, and the venous arteries (pulmonary veins). Additionally, Galen detailed the various orientations of the cardiac myocytes.

By the 2nd century, it was already accepted by some that the heart was comprised of four chambers. However, following the tenets of his predecessor, Erasistratus of Chios, the atria were viewed as extensions of the great vessels penetrating the ventricles, which were regarded as the heart proper [15]. He believed that these thin-walled auricles acted as elastic reservoirs which prevented rupture of the vessels at their insertion into the ventricle when they came under pressure [9]. In his works, he detailed the differences in the wall thickness between the left and right ventricles; the "sigmoid membranes which opened into the great artery; " the trabeculae carnae, and the tricuspid valves [15]. However, he incorrectly concluded that there were perforations in the septum which acted as another means of communication between the ventricular chambers, which he thought existed "for the mutual exchange of blood and pneuma" [17].

Galen used the differences in the structure of the ventricles to support this theory with the thicker left ventricle acting as reinforcement against the weight of the blood-filled right ventricle [7]. Nonetheless, he was the first physician to accept that the arteries carry blood, in addition to "air" [15,16]. He demonstrated this through experiments where he ligated arteries, which were tied on both ends, revealing blood. Moreover, he penetrated the left ventricle to reveal that Herophilus' "pneumatic" ventricle also contained blood. Thus, he incorporated his current findings with the "pneumatism" theory proposed by scholars before him, in particular, the tripartite theory, that is, the three pneumata/vital spirits laid out by Plato [11]. Galen also provided a detailed description of the coronary arteries; however, he wrongly believed that coronary veins were responsible for providing nourishment to the heart [11].

Additionally, Galen accepted the invisible structures proposed by Erasistratus, referring to the existence of the capillaries, and the differences between the veins and arteries [15]. It is ironic that Galen, a believer of teleology: "means do not lead to ends, but ends to means," would come to such a correct "end," while still proposing an incorrect "means." With regards to the circulation of blood and pneuma, Galen held that it was achieved by the bidirectional movement between arteries and veins which were connected by these invisible structures. Moreover, the overall direction of flow of the blood was determined by attraction from the organs in demand. The individual organs were then responsible for the assimilation, retention, and elimination of the blood and its vital "air." This theory would prevail and remain unchallenged through the Renaissance [11].

Based on his suggestion of capillaries, some authors credit Galen with the description of the pulmonary circulation as the following excerpt is found in his writings:

> "The vein-like arteries *[pulmonary veins]* take up a certain portion of blood from the artery-like veins *[pulmonary artery branches]* through subtle and invisible passages"
>
> -Pasipoularides, 2014 [11].

However, it is clear that Galen concluded that the lungs assimilated the blood delivered to it via the pulmonary artery, with only an insufficient amount making its way to the left ventricle via the pulmonary veins. Instead, it was the invisible pores in the interventricular system that allowed blood to enter the left ventricle from the right [15].

Galen also referred to the existence of the ductus arteriosus, as he noticed a communication between the aorta and pulmonary trunk; and the foramen ovale, passage connecting the pulmonary veins with vena cava. Galen also described the "ovale fossa" as the membrane covering the communication "fossa." Under the influence of Herophilus, Galen thought that the tendinous chordae and papillary muscles, to which he referred as "bonds" contracted during diastole to open the valves. He further postulated that these "bonds" were mostly responsible for systole [9].

Despite his invaluable contribution to cardiac anatomy, Galen erroneously accepted the following philosophies: imbalance of humor being the source of disease and evil, in addition to, the heart's function as a distributor of the spirit [16].

Despite having many students, Galen had no anatomical successors. Thus, he took to his grave a lot of his exact surgical methods. Due to the fall of the Western Empire in 476 AD, his work was unfortunately mostly forgotten. The fall of the Western Empire also meant the stagnation of intellectual progression in the West for the next seven centuries. However, during this time the nation of Islam arose [18], resurrecting in its wake, the works of the ancient Greeks [16].

8. Middle ages (5th - 15th centuries)

The Dark Ages are typically regarded as a time of dire living conditions, devastating epidemics, and stifled academia. Despite this infamous recognition, however, the middle ages contributed significantly to medicine and medical knowledge [16].

8.1. 9th - 11th century

During this period, academia and inquiry were stifled by religious authorities. Thus, physicians relied on the work produced by the ancient Greek philosophers and doctors. With regards to anatomy, anatomical dissection was illegal, as a result, the description offered by Galen was taken to be complete and accurate.

While Christians in the West condemned "sensible knowledge" viewing it as imperfect, Arabs in the East organized and translated the work of the ancient Greats such as Galen and Hippocrates from Greek to Arabic [16,18]. The 9th - 12th century is therefore known as the "Golden Age of Islam."

Notable Arabian physicians include Haly Abbas, Avicenna, and Ibn Al-Nafis [16]. During the 10th century A.D., Haly Abbas, a prominent physician to the King of Persia, produced his most significant contribution to anatomy: "Kamil al-al sina'ah-Tibbiyah," which translates into: "The Complete Book of Medical Art." It is also known as "The Royal Book" [16]. Haly Abbas is credited as being the first person of his time to critically evaluate and ultimately reject some of the works of Aristotle and Galen [9]. With regards to the anatomy of the heart Ranhel and Mesquita [16], regards him as the first to distinguish between veins and arteries, and the first to mention the connection between these two vessels. Given the fact that other "anatomists" of Greek antiquity have been shown to make these claims, we belief that this claim of being the first is with regards to the limited knowledge that their society had access to at that time. Moreover, he is also said to have given an in-depth description of the descending aorta. Haly Abbas recognized the heart as a two-chambered organ, with the left chamber being the origin of the arteries, while the veins originated from the liver. He also addressed the following structures: atria, auricles, atrioventricular valves and the presence of the pericardium [16]. Haly Abbas' most significant contribution was the description of the blood supply to the heart, the coronary vessels, which he recognized originated from the aorta [5].

In the 11th century, Haly Abbas was succeeded by Avicenna, also known as Ibn Sina [19]. Avicenna is considered to have been the most revolutionary intellect in both the East and the West, in the West he was known as the "prince of physicians" [19]. During his lifetime, he has contributed more than 450 books on a range of subject matter, ranging from astronomy to medicine. In particular, he made significant strides as it related to the cardiovascular system specifically with regards to his work: "Canon of Medicine" [16]. This text remained the standard in both the East and West until the 16th century [19]. Similar to Haly Abbas before him, he too conceded that the arteries arrived from the left ventricle and the veins from the liver. He also addressed the differential thickness before the walls of the ventricle. Additionally, he is regarded as the first to address the differences in the contraction of the atria and ventricles. Avicenna also advanced the understanding of some of the pathological diseases of the heart and the clinical importance of the radial arterial pulse [16].

Due to the significant contention between the Christian West and the Arab East, there was little exchange of knowledge. However, Italy housed a commercial hub which acted as a peaceful point of contact between the two worlds. This allowed for the entry of translated Arabic scrolls into the western Christian world; scrolls which would reshape the way the west viewed the body and practiced medicine. Some of the knowledge gained from these scrolls were later coveted as original discoveries by some of the "greats" of the West [16].

8.2. 12th - 13th century

In the 13th Century, Ibn-Al-Nafis made significant contributions to the cardiovascular system. He too is regarded to have challenged the "truth" presented by the Greeks [16]. He refuted Galen's claim that the heart was made up of three ventricles. Instead, he recognized only two ventricles which he addressed in his famous book: "Commentary on the

Anatomy of the Canon of Avicenna" [20]. Moreover, Ibn Al-Nafis is credited with being the first to describe the cardiopulmonary circulation. He contended that the septum had no perforations; so, to get from the right side of the heart to the left, the ejected blood traversed the pulmonary circulation. In the pulmonary circulation, the blood was oxygenated before being returned to the left side of the heart [16].

The shift towards the value of knowledge in the West became institutionally evident by the establishment of several universities such as those in "Padua, Montpellier, Oxford, and Bologna" [21]. This shift towards institutionalized knowledge came with the expansion of cities [16]. The milestone of the 13th century that would once again ignite the flame that would progress medicine, in particularly anatomy, came in 1231 when Frederick II (Emperor of the Holy Roman Empire) decreed that medical students be allowed to dissect one human body every five years [21].

8.3. 14th century

However, despite this ruling in the 13th century, no statutory regulations were put in place for the delivery of bodies until 1387. In 1387, the University of Florence requested the provision of the bodies of three incarcerated, alien criminals each year for dissection [22]. Nonetheless, the decree was enough to allow for the controversial "Restorer of Anatomy:" Mondino de Luzzi to live and work [21]. Imagine a professor reading Galen's book aloud as he led a public dissection, which was being performed by a demonstrator. This was the scene of one Mondino's "anatomy classes; " this made him the first to perform public dissections after Herophilus and Erasistratus in the 3rd century B.C [21]. Before dissection Mondino often said:

> "I will teach you the knowledge (*notitia*) of the body not through pointing *ex cathedra*, but rather through hands-on operation (*manualis operatio*) … We must first have knowledge of the whole, and second of the parts … the whole is a composite of its parts, we must begin from an understanding of the whole."
>
> -as cited in Frampton, 2008 [23].

This scene is partially the root of the contention with regards to Mondino's contributions to anatomy. According to critics, Mondino did not dissect any of the specimens himself. Furthermore, findings which contradicted Galen's descriptions were regarded as "morphological transmutation" [21]. However, some of his students contend that he did indeed dissect. Regardless of whether he dissected or not, Mondino produced the anatomical book: "Anathomia." This book offered the first topographical assessment of the organs of the body as it addressed the relationship with neighboring structures, shape, size, texture, physiology, and pathology [21]. However, with regards to the heart, Mondino mistakenly forwarded Aristotle's three chamber theory, in which he conceived that three chambers existed, and the middle chamber was for the creation of the "vital spirit" from blood [21].

While Mondino was by no means the first to perform human dissections, his work represented a renaissance in the study of the human body with the incorporation of dissection into the school's curriculum [24]; thus, earning him the name "Restorer of Anatomy" [21].

9. Late 15th century - 16th century

While Mondino might have lit the first spark in the blazing fire that became the "Renaissance," it was Leonardo da Vinci who was regarded by Feud as the man who "woke up too soon in the darkness while others slept" [14]. Leonardo's contribution to the Renaissance was so significant that Pasipoularides [14] highlights that the "High Renaissance" coincides with Leonardo's most productive years. Andrea del Verrocchio mentored Leonardo Da Vince in the fine arts. Verrocchio's workshop was a hub of intellectual exchange and curiosity. Thus, while Leonardo was mentored in the arts, he became an autodidact in the natural sciences and engineering. The rediscovery of Galen's lost work "De anatomicis administrationibus (On anatomical procedures)" led to an interest in anatomical research versus simply the reteaching of "Anatomy." In Leonardo's later life, Marcantonio della Torres influenced his interest in functional medical anatomy. At that time, illustrations were thought to compromise the authority of anatomical texts. However, Leonardo contended that one should not:

> *"Encumber oneself with words unless speaking to the blind. As. functional anatomic illustration effectively gives synoptic knowledge impossible to convey without multiple tedious dissection cases or, perhaps verbosity of text"*
>
> - [14].

Thus, Psaipoularides [14] suggests that Leonardo is the "originator of modern medical morphophysiological illustration." Moreover, he was the first to offer 3-dimensional constructs from multiple angles, in addition to multiple planar sections. Additionally, he was able to use his inept skills to demonstrate functional anatomy.

Da Vinci took a particular interest in the heart. He was the first to describe the moderator band [25], the two atria (also known as the extrinsic ventricles), and to provide an anatomical drawing of the coronary vasculature, including the great cardiac vein. Additionally, he was the first to describe the pathological changes associated with atherosclerosis. With regards to the physiology of the heart, da Vinci drew on principles outlined by the "Doctrine of Final Cause," which was created by Aristotle and modified by Galen. This doctrine postulated that final cause did not allude to the end, but rather, it alluded to the ultimate cause [14]. Thus, through his investigation of fluid dynamics, he laid the foundation for future physiological breakthroughs. However, like many before him, his interpretation of the function of the heart was misconstrued as he concluded that the heat functioned to produce "vital heat" created from the friction of the blood in momentum. Nonetheless, he accurately recognized that the heart was an actual functioning muscle, which was innervated by branches of the vagus nerve. Leonardo was the first to discover the 4-chamber heart, as we know it today. In addition to the widely accepted "intrinsic" ventricle, he recognized the two atria, which he referred to as the "extrinsic" or upper ventricles [14]. da Vinci also appreciated the difference between the atria and the auricles, the latter to which he referred to as ears/auricular appendage [5]. He was also the first to appreciate that the atria actively expelled blood into the receiving ventricles. However, he incorrectly held on to Galen's principles of the valves functioning as a two-way valve, and the communication of the ventricles through the interventricular septum via pores. Additionally, through poorly designed experiments he incorrectly presented his version of the events during a cardiac cycle [14]. In his works, Leonardo was noted to have described the foramen ovale, the H-shaped upper surface of the mitral valve, the vaulted appearance of the tricuspid valve, in addition to the associated papillary muscles and the chordae tendinae [9].

Irrespective of the few blunders made in his work, da Vinci's greatest oversight might have been his rejection of the value of "print." The result was the production of revolutionary manuscripts which would remain "lost" for centuries [14].

Due to the "hidden" manuscripts of Leonardo, Galen's anatomical theories were considered doctrine until the publication of "*De humani corporis fabrica*" by Andreas Vesalius in 1543. Vesalius was born in the early 16th century. From a very tender age, he demonstrated a profound interest in anatomy as he taught himself anatomy via the dissection of small animals such as mice, and moles [26]. During medical school, the young Vesalius had become so skillful that he was elicited to perform public dissections. He openly shunned those who unquestionably accepted Galen's work without performing their own dissections, which led to the production of his celebrated treatise "On the Fabric of the Human Body (Fabrica)." Such a book represented the "renaissance" of anatomy, as it called "anatomists" of the time to value and validate anatomy using human observation, versus the sole reliance on the “doctrine” of ancient authorities [26]. However, this production was regarded as heresy by the Galenists of the time [27]. The social backlash was so severe that Vesalius left the academic life and became a physician [26].

Despite the brilliance of the Fabrica, with regards to the structure of the heart, Vesalius made some errors. He regarded the heart as a two chambered structure, with the atrium representing dilation of the great vessels. However, Vesalius did not accept Galen's proposal that the ventricular septum contained pores. Moreover, he provided vivid descriptions of some of the structures. For example, based on the left atrioventricular valve resembling a bishop's miter (headdress), he suggested that the valve be named “mitral” [9,26]. Vesalius also managed to design an illustration of the fossa ovalis, which was described by his teacher Jacobus Sylvius [9]. Outside of that published in the *Fabrica*, in 1561, Vesalius, alongside Fallopius, addressed the presence of the “ductus arteriosus” [28]. However, the first description of the “ductus arteriosus” was published by Aranzio, a pupil of Vesalius, in a book entitled “De humano foetu libellus” in 1564. In the same year, Leo Botallo referred to the ductus arteriosus as the foramen ovale in his monogram “De catarrho” [9].

Despite challenging the Galenic anatomy, Vesalius offered no alternative view on the proposed physiology [26]. While Vesalius failed to offer any new physiological insight into the heart, his assistant Realdo Colombo correctly described the pulmonary circulation. Moreover, he correctly identified that the aorta and pulmonary artery actually conducting blood out of the heart [9]. He is regarded as being the first to imply that blood-air mixing occurred in the lungs, versus the heart [5]. Colombo also recognized the function of the valves with regards to the direction of blood flow [5].

Another prominent anatomist and surgeon of the 16th century is Giulio Cesare Aranzio. He discovered several structures in the body due to his meticulous nature. With regards to the heart, he is credited with his discovery of the nodes or nodules of Arantius [9].

10. 17th century

The early 17th century saw one of the greatest contributions to “anatomo-physiological” principles: William Harvey's circulation of blood. While Harvey more than likely held onto the two-chambered heart, he recognized the interventricular septum as a nonporous barrier. Moreover, he rejected the Galenic theory that right ventricle solely functioned to provide nutrients via blood to the lungs. He also regarded the heart as the force behind circulation [5].

Despite Aranzio's description of the “ductus arteriosus,” in 1660 Leo Botallo was credited as the discoverer of the ductus arteriosus, and some referred to it as “ductus Botalli.” Credit was given to Botallo since the ductus arteriosus was demonstrated by the anatomist van Home, in a newer edition of Botallo's book. However, this was refuted by Charles Singer because Galen had alluded to the ductus arteriosus in his work. Moreover, in the late 16th century, several authors had already described the ductus arteriosus, with or without illustrations, in their work including Giambattista Carcano and Fabricius ab Aquependente [9].

The intervenous tubercle of Lower is named after its discovery Richard Lower. In 1669, Lower named the swelling “intervenous tubercle” in his book “Tractatus de Corde” [9]. However, in 2012, Loukas et al. [29] contended that Lower was referring to the superior limbus of the fossa ovalis and that no true tubercle existed in the located demarcated by Lower. Lower made other notable contributions such as recognizing the heart was a four chamber, whose contractility was responsible for its circulation. In the Western World, Lower is considered the first to perform a transfusion [5].

11. 18th century

The limbus of the fossa ovalis was initially referred to as the “annulus ovalis.” The limbus was also referred to as the “oval ring of Vieussens” as it was perceived that Raymond Vieussens was the first to describe it in his 1705 book “Traite nouveau de la structure et de la cause du mouvement naturel du Coeur” (Treatise of the Heart). However, as previously addressed, this structure had been described since the 16th century by Jacobus Sylvius. Additionally, the annulus ovalis was also documented by Bartolomeo Eustachio in the textbook “Opuscula Anatomica” in 1564 [9]. In his work, Vieussens also described two other structures which bear his name today: the collateral blood supply to the left side of the heart in the effect of a left anterior descending artery occlusion, and the valve located between the great cardiac vein and the coronary sinus ostium. These two structures are known as “Vieussens' arterial ring,” and “Vieussens’ valve” respectively [5]. “Treatise of the Heart” is also noted to provide a detailed description of the blood supply to the heart, and the coronary sinus. In a later publication, Vieussens also recognized the microcirculation of the venous system to which he referred to as “ducti carnosi” [30].

While Vieussens investigated the blood supply to the heart, his contemporary, Adam Christian Thebesius investigated the venous drainage of the heart. He described the vessels which emptied directly into the chambers of the heart. He subscribed the name “vasa cordis mimima,” these vessels have come to be known as “Thebesian vessels” [5].

In 1740, the aortic sinus was described by Antonio Maria Valsalva in his book “Opera.” Thus, up to this day, it bears his name: Sinus of Valsalva. However, before this, the sinuses were thoroughly investigated by Leonardo da Vinci who constructed glass models to examine the three eddy currents that forced the valve to close [9].

In the latter part of the 18th century, Antonio Scarpa published a collection of tables which outlined his research on the nervous system. In it, he described the innervation of the heart - one of his many achievements [31].

12. 19th century

Despite being first described anatomically and functionally by da Vinci, the moderator band was so named in 1837 by King based on the proposal that like a governor it controlled the capacity of the right ventricle [32]. Nonetheless, due to its original illustrator, it is less commonly referred to as Leonardo's cord [33].

In 1844, centuries after its discovery, the ductus arteriosus was first regarded as a congenital malformation by Karl von Rokitansky. A few years later, Williams and Benutz were the first to relate the murmur with a patent ductus arteriosus. In 1867, Gerhad sorted a possible explanation for this associated and concluded that it was due to turbulence in the pulmonary artery [9]. His and Purkinje discovered the conduction system of the heart in the 19th Century with regards to the structures that bear their names: Purkinje fibers and the bundle of His [5].

By the middle of the 19th century, it was perceived that all the great discoveries of anatomy had already been made. It was thought that to impact anatomy at this stage; a genuinely original piece would need to be created. Henry Gray and Henry Vandyke Carter were able to achieve just that with the publication of their book: “Gray's Anatomy” in 1860. Gray's writings were clear and authoritative, while Carter masterfully produced accurate illustrations. However, sadly, Carter's invaluable contributions, which set the book apart from other texts of the time, is generally undervalued as his name remains unknown [34]. On publication, the book was so well received that looking back the reviews appear prophetic, the British Medical Journal proclaimed that Gray's “… must take its place as the manual of Anatomy Descriptive and Surgical” [35].

More than a century and a half after its first publication, the 41st edition of Gray's Anatomy was published in 2016. Gray's Anatomy, which was created as an anatomical treatise for students continue to be an authoritative source for medical students [36]. Several other anatomical tomes were produced in the mid-nineteenth century; however, none has stood the test of time like Gray's Anatomy [34].

Another great set of publications from the late 19th to 20th was that of the recovered works of da Vinci [37].

13. 20th century

Recognizing the continuous nature of the moderator band with the ridge of muscle originating at the membranous septum, Julius Tandler subscribed the name “trabecula septomarginalis” to these structures in 1913 [38,39]. Retzer and Braeuning, along with Tawara a few years later, added to the earlier description of the conducting system. Tawara is praised for relating the anatomy of the conducting system to its function [5].

As technology advanced in the 20th century, so did medical imaging and treatment modalities. These advancements which relied on the internal tomographic examination of the heart alerted current anatomists to the grave errors that had been made in the past with regards to the anatomical nomenclature of the heart [40]. In 1975, MacAlpine was one of the first to address this need with his publication of his atlas: “Heart and Coronary Arteries.” In this book, he coined the word “attitudinal,” referring to the examination of the heart as it lies in the body, that is, its normal attitude. While scholars from the early 19th century had sorted to address this error, it was not until Cosio et al. [41] demonstrated the clinical implication of these errors for the electrophysiologist that a profound interest was triggered in addressing the nomenclature of the heart in what is known as attitudinally correct.

14. 21st century

Since its renewed interest the late 20th century, authors have continued to investigate the attitudinal position of the heart to offer a complete, and more importantly an accurate description and analysis of the anatomy of the heart. These errors in nomenclature resulted from the examination of the heart in the so-called “Valentine position.” This position saw the heart rotated through one right angle from its true long axis. That is, instead of examining the heart as it lies in the body, anatomists of the past, removed the heart from the body and placed it on its apex in line with the long axis of the body [40].

Thus, when the heart is examined in situ, it becomes clear that some of the structures of the heart which were designated purely anatomical names are not attitudinally correct. Examining the undissected heart in its attitudinal location from the frontal plane, it quickly becomes apparent that all four chambers of the heart are not visible from this plane [40]. Instead, the majority of the anterior surface of the heart is occupied by the right ventricle, with the right atrium lying superior to the right ventricle. Given this fact, combined with the fact that only 1/3rd of the heart mass lies to the right [42], attitudinally correct nomenclature is needed for the chambers of the heart. Thus, when taken as a unit, the chambers should have been named as follows: right atrium-antero-superior, right ventricle - anterior ventricle, left atrium - posterior atrium, and left ventricle - inferior ventricle [40]. The left ventricle is regarded attitudinally as the inferior ventricle, as in the body, the majority of the free wall of the left ventricle actually lies on the diaphragm, which is inferior to the heart. Since the “posterior interventricular artery” traverses this surface in the “posterior interventricular groove,” it follows that both the groove and artery should bear the name “inferior” [43]. Even the name of the “anterior interventricular groove” has been challenged as it does not lie truly anterior, but rather it lies more superior, anterior, and to the left. Thus, the groove and the artery which occupies it are more correctly described as “antero-superior” interventricular sulcus/artery [43].

On examination of the internal structures of the heart, attitudinally corrected nomenclature has been suggested for the following structures: atrioventricular valves and their associated papillary muscles, semilunar valves, and the septum. The leaflets of the tricuspid valves are more accurately regarded as antero-superior, inferior, and septal. Their associated attaching papillary muscles should be named as follows: anterior, posterior, and septal respectively. Similarly, a name change is required for their left counterpart as the left leaflets are positioned anterosuperior and posteroinferior. These leaflets attach to the superolateral and inferoseptal papillary muscles respectively [1].

Strides towards the widespread acceptance of attitudinally correct nomenclature has been made as the recent edition of the highly proclaimed Gray's Anatomy has been published with the updated cardiac nomenclature.

15. Conclusion

The anatomy of the heart has been a slow and steady journey, traveled by intellects of various background, who remained painstakingly committed in their pursuit of the “truth” despite various challenges. We recognize that a complete history of the anatomy of the heart is elusive due to works which have been lost, intentionally or inadvertently. Nonetheless, it is beneficial to reflect on this point as it reminds us that not every “doctrine” represents truth.

Ethical statement

This paper has been written to the highest ethical standards.

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